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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,774	12/08/2005	Sara Brett	VB60547	1360

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EXAMINER	
HUMPHREY, LOUISE WANG ZHIYING	
ART UNIT	PAPER NUMBER
1648	

NOTIFICATION DATE	DELIVERY MODE
05/14/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/534,774	BRETT ET AL.	
	Examiner	Art Unit	
	LOUISE HUMPHREY	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 15-19* is/are pending in the application.

4a) Of the above claim(s) *7,8,12,13,18 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,9-11 and 15-17* is/are rejected.

7)☒ Claim(s) *9-11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 May 2005* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/13/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 14 and 20 are cancelled. Claims 1-13 and 15-19 are pending.

Election/Restriction

Applicant's election without traverse of (1) Group I, claims 1-17; and (2) the species of HCV NS3-core(1-151) fusion in the first cassette with NS4B-NS5B fusion in the second cassette, in the reply filed on 07 February 2008 is acknowledged.

Claims 7, 8, 12, 13, 18 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions and species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07 February 2008.

Claims 1-6, 9-11 and 15-17 are examined to the extent that they read on the elected species.

Priority

It is noted that this application appears to claim subject matter disclosed in prior Application No. PCT/EP03/12793, filed on 13 November 2003. Therefore, the effective filing date is deemed to be 13 November 2003.

Receipt is acknowledged of papers submitted under 35 U.S.C. §119(a)-(d), which papers have been entered. Therefore, the priority date is deemed to be the filing date of the foreign priority application UNITED KINGDOM 0226722.7 (11/15/2002).

Information Disclosure Statement

Applicant's Information Disclosure Statements (IDS) filed on 13 May 2005 (two pages total) has been received and entered into the application. As reflected by the attached, signed copy of form PTO-1449A, the Examiner has considered the cited references.

Specification

Content of Specification

(a) Title of the Invention: See 37 CFR 1.72(a) and MPEP § 606. The title of the invention should be placed at the top of the first page of the specification unless the title is provided in an application data sheet. The title of the invention should be brief but technically accurate and descriptive, preferably from two to seven words may not contain more than 500 characters.

(b) Cross-References to Related Applications: See 37 CFR 1.78 and MPEP § 201.11.

(c) Statement Regarding Federally Sponsored Research and Development: See MPEP § 310.

(d) The Names Of The Parties To A Joint Research Agreement: See 37 CFR 1.71(g).

(e) Incorporation-By-Reference Of Material Submitted On a Compact Disc: The specification is required to include an incorporation-by-reference of electronic documents that are to become part of the permanent United States Patent and Trademark Office records in the file of a patent application. See 37 CFR 1.52(e) and MPEP § 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text were permitted as electronic documents on compact discs beginning on September 8, 2000.

(f) Background of the Invention: See MPEP § 608.01(c). The specification should set forth the Background of the Invention in two parts:

(1) Field of the Invention: A statement of the field of art to which the invention pertains. This statement may include a paraphrasing of the applicable U.S. patent classification definitions of the subject matter of the claimed invention. This item may also be titled "Technical Field."

(2) Description of the Related Art including information disclosed under 37 CFR 1.97 and 37 CFR 1.98: A description of the related art known to the applicant and including, if applicable, references to specific related art and problems involved in the prior art which are solved by the applicant's invention. This item may also be titled "Background Art."

(g) Brief Summary of the Invention: See MPEP § 608.01(d). A brief summary or general statement of the invention as set forth in 37 CFR 1.73. The summary is separate and distinct from the abstract and is directed toward the invention rather than the disclosure as a whole. The summary may point out the advantages of the invention or how it solves problems previously existent in the prior art (and preferably indicated in the Background of the Invention). In chemical cases it should point out in general terms the utility of the invention. If possible, the nature and gist of the invention or the inventive concept should be set forth. Objects of the invention should be treated briefly and only to the extent that they contribute to an understanding of the invention.

(h) Brief Description of the Several Views of the Drawing(s): See MPEP § 608.01(f). A reference to and brief description of the drawing(s) as set forth in 37 CFR 1.74.

(i) Detailed Description of the Invention: See MPEP § 608.01(g). A description of the preferred embodiment(s) of the invention as required in 37 CFR 1.71. The description should be as short and specific as is necessary to describe the invention adequately and accurately. Where elements or groups of elements, compounds, and processes, which are conventional and generally widely known in the field of the invention described and their exact nature or type is not necessary for an understanding and use of the invention by a person skilled in the art, they should not be described in detail. However, where particularly complicated subject matter is involved or where the elements, compounds, or processes may not be commonly or widely known in the field, the specification should refer to another patent or readily available publication which adequately describes the subject matter.

(j) Claim or Claims: See 37 CFR 1.75 and MPEP § 608.01(m). The claim or claims must commence on separate sheet or electronic page (37 CFR 1.52(b)(3)). Where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP § 608.01(i)-(p).

(k) Abstract of the Disclosure: See MPEP § 608.01(f). A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the claims. In an international application which has entered the national stage (37 CFR 1.491(b)), the applicant need not submit an abstract commencing on a separate sheet if an abstract was published with the international application under PCT Article 21. The abstract that appears on the cover page of the pamphlet published by the International Bureau (IB) of the World Intellectual Property Organization (WIPO) is the abstract that will be used by the USPTO. See MPEP § 1893.03(e).

(l) Sequence Listing, See 37 CFR 1.821-1.825 and MPEP §§ 2421-2431. The requirement for a sequence listing applies to all sequences disclosed in a given application, whether the sequences are claimed or not. See MPEP § 2421.02.

The disclosure is objected to because of the following informalities:

(1) Missing Description of Figure 6

The specification is missing a description of drawings section. Figure 6 is not described anywhere in the specification although Figures 1-5 and 7-23 are mentioned in the specification as follows:

Figure 1: page 2, line 9; and page 15, line 4;
Figure 2 to Figure 5: page 11, lines 15-21;
Figure 7: page 26, line 46;
Figure 8: page 28, line 12;
Figure 9: page 28, lines 19-20;
Figure 10: page 28, line 28;
Figure 11: page 29, line 11;
Figure 12: page 30, line 15;
Figure 13: page 32, lines 21-23;
Figure 14: page 35, line 2;
Figure 15: page 35, line 11;
Figure 16: page 36, line 9;
Figure 17: page 37, line 11;
Figure 18: page 37, line 19;

Figure 19: page 37, line 22;
Figure 20: page 39, line 3;
Figure 21: page 40, line 4;
Figure 22: page 41, line 1;
Figure 23: page 41, line 7.

(2) Sequence Compliance

The specification and drawings are objected to for failing to adhere to the requirements of the sequence rules. Applicant must append SEQ ID NO's to all mentions of specific sequences in the specification (pages 26-27 and 34) and the drawings. See 37 CFR § 1.821(d). Full compliance is required in response to this Office Action. A reply that fails to comply will be considered to be non-responsive and may result in ABANDONMENT of this application.

(3) Drawings in the Specification

The specification shall not contain drawings or flow diagrams. See 37 C.F.R. 1.58(a). The specification contains numerous diagrams on page 8, 12, 13, 29, 30 and 36.

Appropriate correction is required.

Claim Objections

Claims 9-11 are objected to because they depend from a nonelected claim.

Appropriate correction is required.

Double patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 10 of copending Application No. 10/535047. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claim 1 is anticipated by claim 10 of the Application No. 10/535047. The instant claim encompasses the copending claim, and vice versa.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112, 1st ¶, scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 9-11 and 15-17 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a polynucleotide, does not reasonably provide enablement for a vaccine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Additionally, claims 2 and 17 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for a polynucleotide, does not reasonably provide enablement for a vaccine.

In making a determination as to whether an application has met the requirements for enablement under 35 U.S.C. §112, first paragraph, the courts have put forth a series of factors (MPEP §2164.01(a)). See, *In re Wands*, 8 USPQ2d 1400, at 1404 (CAFC 1988); and *Ex Parte Forman*, 230 U.S.P.Q. 546 (BPAI 1986). The factors that may be considered include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. *Id.* While it is not essential that every factor be examined in detail, those factors deemed most relevant should be considered.

The nature of the invention is a DNA-based HCV vaccine. The breadth of the claims extends to protection against any strain of HCV by the recited polynucleotide

vaccine. The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

The specification provides little guidance regarding practice of the claimed methods. The specification, at most, describes the immunogenic effects of the claimed polynucleotides after expression in cells and in mice. However, the specification does not disclose the protective effect against HCV, if any, of expressing any of the recited polynucleotides in a cell or a subject.

The disclosure fails to provide any working examples that meet the claimed limitation of a "vaccine." Despite of the one cell culture example and murine models demonstrating the immune response elicited by the claimed polynucleotide (page 30-35), there are no examples of challenge studies of the immunized cells or animals with any strain of HCV that indicates the prevention of HCV infection after a subject receives the claimed polynucleotide vaccine. In conclusion, Applicants have not provided any evidence that confirms vaccine efficacy of the HCV double-cassette polynucleotide. Thus, the disclosure does not remotely relate to prevention against the infection of any strain of HCV in any subject, especially in humans. Therefore, the disclosure is not commensurate in scope with the claimed invention.

Viral diversity and genetic heterogeneity in hepatitis C virus (HCV) infection and other viral diseases play an essential role in viral immune escape and the development of chronic infection. Despite this knowledge most vaccine approaches against HCV have excluded this important issue. Moreover the feasibility of developing an effective HCV vaccine has been questioned, mainly because prophylactic immunity against HCV

cannot be achieved in chimpanzees by either vaccination or previous HCV infection, and re-infection in men has been reported, most likely due to genetic shift and immune escape (Encke, 2007). The importance of mutant viruses in pathogenicity, immunity, natural history, clinical outcomes, vaccine production, and responsiveness to treatment need to be addressed before a vaccine can be successfully developed. The current state of art teaches three factors that may affect the effectiveness of antiviral therapies: (1) immune escape by mutations, (2) inhibition of antigen presentation, and (3) inhibition of interferon signaling in hepatocytes (Ahlen, 2005). Although the immunogenicity of DNA plasmids encoding HCV protein(s) is known in the art (Ou-Yang, 2002), there is little information on correlates of immunity. Even a previously established epitope can lose its immunogenicity due to mutational viral escape, as seen with the E1 DNA vaccine studied by Encke *et al.* (2007). The prior art is unpredictable and fails to provide sufficient illumination pertaining to the relationship between immune response and protection or prevention from infection. Because of these uncertainties, and even greater uncertainties related to the amount of virus transmitted, the site and cell type involved in initial replication, and the kinetics of virus dissemination, the ability of currently available *in vitro* or *in vivo* immunoassays to reliably predict vaccine efficacy is questionable.

An ideal HCV vaccine should prime cross-neutralizing anti-HCV protein antibodies, and provide broad HCV-specific helper and inflammatory CD4+ T cell responses, as well as HCV-specific cytotoxic CD8+ T cell responses (Abrignani, 1999). The working example provided in the specification does not evaluate the complete

panel of immune response, thus, it is uncertain whether the claimed double-cassette HCV polynucleotide meets the criteria of an effective HCV vaccine. It is pure speculation on Applicant's part that the double-cassette polynucleotides set forth can prevent the infection of any strain of HCV in any subject given that the state of the art of "HCV vaccine" is undeveloped. There is little specific guidance in the art or specification and no specific examples of protection set forth in the specification. While Applicant is not required to set forth working examples, the specification must set forth sufficient teachings to allow one to practice the claimed invention. The only working example is Example 5, which is not commensurate in scope with the claimed invention. There is no evidence that the polynucleotides prepared by the claimed method will actually be suitable as a HCV vaccine. Absent data addressing the problems that well known in the development of HCV vaccine and validating the protective effect of the claimed HCV double-cassette polynucleotides, one skilled in the art is left with undue and unpredictable experiment to obtain the claimed invention. Thus, the instant invention, based on the evidence as a whole, in light of the factors articulated by the court in *In re Wands*, lacks an enabling disclosure.

Legal precedence dictates that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification. *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18 24 (C.C.P.A. 1970). *In re Vaeck*, 20 U.S.P.Q.2d 1438 (C.A.F.C 1991). *In re Angstadt*, 537 F.2d 498, 502-03, 190 U.S.P.Q. 214, 21 (C.C.P.A. 1976). Thus, when all the aforementioned factors are considered *in toto*, it would

clearly require undue and unpredictable experimentation from the skilled artisan to practice the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 1-5, 15 and 16 are rejected under 35 U.S.C. §103(a) as being unpatentable over Chien *et al.* (US 6,261,764 B1, patented on 17 July 2001, "Chien") in view of Glenn *et al.* (US 2006/0199174 A1, effectively filed one 22 August 2003).

The instant claims are directed to a codon-optimized HCV polynucleotide of two expression cassettes *in cis*, the first expression cassette encoding the HCV core protein is downstream of the second expression cassette encoding at least one other HCV protein.

Chien discloses a DNA expression cassette encoding the HCV proteins, NS3-NS4B-NS5B-core, wherein the core protein is a truncated fragment consisting of amino acids 10-53 downstream of the nonstructural (NS) proteins and the nonstructural proteins contain multiple epitopes (column 5, line 11-53), which meets the limitation of mutated core protein wherein the mutation reduces expression of the core protein.

Chien does not disclose the core protein in a second expression cassette and is implicit on the part that the epitopes encoded by the DNA cassette are codon-optimized.

Glenn discloses that single and dual expression cassette vectors are well known in the art (page 8, paragraph [0073]). Glenn also suggests codon optimization of HCV nucleic acids or polynucleotides for expression in mammalian cells (page 8, paragraph [0072]).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Chien polynucleotides so as to include a second expression cassette encoding the truncated core protein and optimize the codons of the polynucleotides for expression in cells of mammalian cells. The skilled artisan would have been motivated to do so to ensure that the core protein is expressed at the same time as the nonstructural HCV fusion proteins (NS4B-NS5B) but as a separate protein in the same cell. This way, both anti-core and anti-NS immune responses can be simultaneously elicited and/or detected. There would have been a reasonable expectation of success, given the art-recognized practice of DNA plasmids with dual expression cassettes, as taught by Glenn. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 1-6, 9-11 and 15-17 are rejected under 35 U.S.C. §103(a) as being unpatentable over Chien *et al.* (US 6,261,764 B1, patented on 17 July 2001, "Chien") in view of Glenn *et al.* (US 2006/0199174 A1, effectively filed one 22 August 2003) and Shah *et al.* (US 6,727,092 B2, filed on 17 July 2002, "Shah").

The instant claims are directed to a codon-optimized HCV plasmid of two expression cassettes *in cis*, the first expression cassette, encoding NS3 fused to a C-

terminal truncated HCV core protein consisting of amino acids 1-151, is downstream of the second expression cassette encoding NS4B-NS5B fusion protein.

Chien discloses a DNA expression cassette encoding the HCV proteins, NS3-NS4B-NS5B-core, wherein the core protein is a truncated fragment consisting of amino acids 10-53 downstream of the nonstructural (NS) proteins and the nonstructural proteins contain multiple epitopes (column 5, line 11-53).

Chien does not disclose the HCV core protein in a second expression cassette, nor the fusion of HCV NS3 with a truncated core protein consisting of amino acids 1-151. Chien is implicit on the part that the epitopes encoded by the DNA cassette are codon-optimized.

Glenn discloses that single and dual expression cassette vectors are well known in the art (page 8, paragraph [0073]). Glenn also suggests codon optimization of HCV nucleic acids or polynucleotides for expression in mammalian cells (page 8, paragraph [0072]).

Glenn does not disclose the fusion of HCV NS3 with a truncated core protein consisting of amino acids 1-151.

Shah discloses a plasmid containing codon-optimized sequences of an HCV NS3 segment fused to an HCV core region of amino acids 1-150 (column 18, line 9-12). Shah further discloses that multiple epitopes have been identified within the first 115 amino acids of the native HCV core protein and suggests that recombinant antigens for the detection of anti-core immune responses need only contain this portion of the native protein (column 15, line 34-42).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the Chien polynucleotides so as to include a second expression cassette encoding the truncated core protein and optimize the codons of the polynucleotides for expression in cells of mammalian cells. The skilled artisan would have been motivated to do so to ensure that the core protein is expressed at the same time as the nonstructural HCV fusion proteins (NS4B-NS5B) but as a separate protein in the same cell. This way, both anti-core and anti-NS immune responses can be simultaneously elicited and/or detected. There would have been a reasonable expectation of success, given the art-recognized practice of DNA plasmids with dual expression cassettes, as taught by Glenn.

It would have been further obvious to one of ordinary skill in the art at the time the invention was made to modify the Chien polynucleotides so as to include a second expression cassette encoding the NS3B tether to a truncated core protein of amino acids 1-150, as taught by Shah. The skilled artisan would have been motivated to do so to optimize the expression of all four antigens so as to increase the amount of immune response, especially since the NS3-core(1-150) is routinely used in multiple commercial assays for the detection of HCV, as taught by Shah.

The Shah HCV core protein fragment (amino acids 1-150) differs from the claimed HCV core fragment (amino acids 1-151) by only one amino acid residue, which renders the claimed invention obvious since the minor change in chemical configuration or design of molecule discovered or made by applicants is *de minimis*, since there is no evidence that amino acid 151 of HCV core protein is essential for immunogenic activity,

and since applicants have not explained practical advantages of any differences in the structure between claimed HCV core protein fragment and the prior art. See *Ex Parte Anderson* 30 USPQ2d 1866 (Bd. Pat. App. & Int. 1993).

Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claim is allowable.

Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP §714.02 and §2163.06.

Correspondence

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louise Humphrey, Ph.D. whose telephone number is 571-272-5543. The examiner can normally be reached on Mon-Fri, 9:30 am - 5:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/L. H./
Examiner, Art Unit 1648

/Bruce Campell/
Supervisory Patent Examiner, Art Unit 1648